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January 25, 2008

GOWLING LAFLEUR HENDERSON LLP

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Application No. : 2,491,680
Owner : SOUTHERN RESEARCH INSTITUTE
Title : INHIBITORS OF FTSZ AND USES THEREOF
Classification : A01N 43/42 (2006.01)
Your File No. : 08902107CA
Examiner : Ingrid Popesku

YOU ARE HEREBY NOTIFIED OF A REQUISITION BY THE EXAMINER IN ACCORDANCE WITH SUBSECTION 30(2) OF THE PATENT RULES. IN ORDER TO AVOID ABANDONMENT UNDER PARAGRAPH 73(1)(A) OF THE PATENT ACT, A WRITTEN REPLY MUST BE RECEIVED WITHIN **6** MONTHS AFTER THE ABOVE DATE.

This application has been examined taking into account the:

Description, pages 1-92, as originally filed;
Claims, 1-42, as originally filed; and
Drawings, pages 1/9-9/9, as originally filed.

The number of claims in this application is 42.

A search of the prior art has revealed the following:

References Applied:

PCT Application

0174788 11 October 2001

Brooks et al. ✓

Publications

Suling et al., "Antimycobacterial activity of 1-deaza-7,8-dihydropteridine derivatives against *Mycobacterium tuberculosis* and *Mycobacterium avium* complex *in vitro*", Journal of Antimicrobial Chemotherapy (2001), 47, 451-454

Leung et al., "Crystallization of the *Mycobacterium tuberculosis* cell-division protein FtsZ", Acta Crystallographica Section D: Biological Crystallography (2000), D56(12), 1634-1637

Cho et al., "New anti-MRSA cephalosporins with a basic aminopyridine at the C-7 position", Bioorganic & Medicinal Chemistry Letters (2001), 11, 137-140

Didier et al., "Screening of compounds for antimicrosporidial activity *in vitro*", Folia Parasitologica (1998), 45, 129-139

Brooks et al. disclose 2-(S)-hydroxymutilin carbamate derivatives which correspond to those compounds of claims 1, 21 and 37 of the present application that are useful in the treatment of bacterial infections (see Preparation 3, Examples 1(a), 1(b), 2, 4, 11, 23 and 39).

Suling et al. disclose compounds which correspond to those of the present application of claims 1, 12-16, 21 that exhibit antimycobacterial activity against *Mycobacterium tuberculosis* (see Table I, compound 1-5, 7-9 and 11).

Leung et al. disclose the compound SRI-7614 (page 1634) for the inhibition of *Mycobacterium tuberculosis* FtsZ (MtbFtsZ).

Cho et al. disclose compounds that correspond to those of the present application of claim 1 and 21 for the inhibition of methicillin-resistant *Staphylococcus aureus* (MRSA) (see compounds 4, 8, 10-16).

Didier et al. disclose the compounds SRI-7462 and SRI-7614 (see Table 2) for the inhibition of *Encephalitozoon intestinalis*.

The examiner has identified the following defects in the application:

Claims 1-6, 21-25 and 37-41 do not comply with paragraph 28.2(1)(b) of the *Patent Act*. Brooks et al. disclosed the claimed subject matter before the claim date.

Claims 1-4, 11-16, 21-23 and 26-29 do not comply with paragraph 28.2(1)(a) of the *Patent Act*. The subject-matter defined by these claims was disclosed by Suling et al. more than one year before the filing date of the present patent application.

Claims 1-4, 11, 13, 17, 18, 20-23 and 26-29 do not comply with paragraph 28.2(1)(a) of the *Patent Act*. The subject-matter defined by these claims was disclosed by Leung et al. more than one year before the filing date of the present patent application.

Claims 1-4, 11 and 21-23 do not comply with paragraph 28.2(1)(b) of the *Patent Act*. Cho et al. disclosed the claimed subject matter before the claim date.

Claims 1-3, 11, 13-18, 20-22 and 26 do not comply with paragraph 28.2(1)(b) of the *Patent Act*. Didier et al. disclosed the claimed subject matter before the claim date.

Claims 1-19, 21-35, and 37-42 are broader in scope than the teaching of the description. To comply with Section 84 of the Patent Rules, the Examiner respectfully submits that the antibacterial compounds of claims 1-19, 21-35 and 37-42 be limited to when $S_1 (R_1)$ = methyl, ethyl, phenyl and benzyl. There currently is a lack of support in the examples found on pages 31-44 and 48-92 of the description for the compounds of claims 1-19, 21-35 and 37-42 other than those with $S_1 (R_1)$ = methyl, ethyl, phenyl and benzyl. There is no evidence in the present specification to suggest that antibacterial agents other than those of the compounds of claims 1-19, 21-35, 37-45 with $S_1 (R_1)$ = methyl, ethyl, phenyl and benzyl will yield compounds of the claimed utility. In view of the examples, the scope of the above claims are deemed broader than the teaching of the description and should be limited to the antibacterial compounds of claims 1-19, 21-35 and 37-42 be limited to when $S_1 (R_1)$ = methyl, ethyl, phenyl and benzyl.

Claims 1-42 are directed to a method of medical treatment that does not produce an essentially economic result in relation to trade, commerce, or industry, and is therefore outside the definition of invention in section 2 of the *Patent Act*. (See Tennessee Eastman v. Commissioner of Patents (1974) S.C.R. 111, or (1972) 8 C.P.R. (2d) 202, confirmed by Imperial Chemical Industries v. Commissioner of Patents (1986) 3 F.C. 40, or (1986) 9 C.P.R. (3d) 289).

Claims 1, 12-19, 21, 27 and 37 are ambiguous and do not comply with subsection 27(4) of the *Patent Act*. The term "or" before the last element of the specified group causes a lack of clarity, as it is unknown whether the last element is part of said group or not (see Section 11.11 of the Manual of Patent Office Practice).

Claims 1, 12-14, 16-19, 21, 27 and 37 are indefinite and do not comply with Subsection 27(4) of the *Patent Act*. The expression "organic radical comprising 1-8 (26) carbon atoms" is open-ended and as such indefinite. The scope of this expression is impossible to determine.

Claim 11 is indefinite and does not comply with subsection 27(4) of the *Patent Act*. The inclusion of "less than about" causes ambiguity. The starting value for the molecular weight of the compound of claim 1 cannot be ascertained with any confidence, and thus the claim is ambiguous. For the expression "less than about" in claim 11, the term "about" allows for a molecular weight of slightly above or slightly below 500 gm/mole of the compound of claim 1, while the expression "less than" explicitly states that the molecular weight must be less than 500 gm/mole. The simultaneous use of both terms is contradictory and causes uncertainty in the scope of protection afforded by the claimed molecular weight range.

Claim 15 does not comply with subsection 87(2) of the *Patent Rules*. Dependent claims must refer to preceding claims.

The expression disclosed on page 1, lines 5-6 should be removed since this application is a Canadian application.

The y-axis label of Figure 3 is illegible and should therefore be amended.

A statement in an application, such as found on page 11, lines 2-3; page 12, line 11; page 21, line 11; page 23, line 14; page 39, line 22; page 40, line 1 and page 44, line 18 which incorporates by reference any other document, does not comply with subsection 81(1) of the *Patent Rules*.

In view of the foregoing defects, the applicant is requisitioned, under subsection 30(2) of the *Patent Rules*, to amend the application in order to comply with the *Patent Act* and the *Patent Rules* or to provide arguments as to why the application does comply.

Under section 34 of the *Patent Rules*, any amendment made in response to this requisition must be accompanied by a statement explaining the nature thereof, and how it corrects each of the above identified defects.

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GOWLINGS

Patent Prosecution Highway Pilot Program

Commencing January 28, 2008 a pilot program between the CIPO and the USPTO will be in effect. This provides an opportunity for accelerated examination for corresponding applications where there are allowed claims in either jurisdiction. Applicants with a priority filing in one country may be eligible for the pilot program. Information is available at http://strategis.ic.gc.ca/sc_mrksv/cipo/patents/PPH_program-e.html. If you are interested in this program, please contact us.

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IN THE CANADIAN INTELLECTUAL PROPERTY OFFICE

In The Matter of Canadian Patent Application:

Current Owner : **Southern Research Institute**
Original Applicant : **Southern Research Institute**
Serial No. : **2,491,680**
Filing Date : **July 2, 2003**
Title : **Inhibitors Of FtsZ And Uses Thereof**
Our File : **08902107CA**
Date : **JUL 25 2008**

The Commissioner of Patents
50 Victoria Street, Phase I, Place du Portage
Gatineau, Quebec K1A 0C9

Response to Official Action

Dear Commissioner of Patents:

In response to the Official Action dated January 25, 2008, kindly amend this application as follows:

In the Disclosure:

Pages 1, 11, 12, 21, 23, 39, 40 and 44: Amend.

Please substitute attached Disclosure pages 1, 11, 12, 21, 23, 39, 40 and 44 for the corresponding pages presently on file.

In the Drawings:

Drawings page 3/9: Amend.

Please substitute the attached sheet of drawings containing Figure 3 for the corresponding sheet of drawings presently on file.

In the Claims:

Claims 1, 11, 14-17 (now 12-15), 19-21 (now 16-18), 27 (now 24) and 37-42 (now 34-39): Amend.

Claims 12, 13, and 18: Cancel without prejudice or disclaimer.

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Please add new claims 40-82.

The remaining claims and their dependencies have been renumbered accordingly.

Please substitute the attached claims pages 93-119 containing claims 1-82 for the claim pages presently on file.

REMARKS

Reconsideration of this application is respectfully requested having regard to the foregoing amendments and the following comments.

Novelty Objection

The Examiner objected to claims 1-6, 21-25 and 37-41 under paragraph 28.2(1)(b) of the *Patent Act* alleging that Brooks et al. ("Brooks") disclosed the claimed subject matter before the claim date.

Claims 1, 21 (now 18) and 27 (now 24) have been amended to include the structural formula of claim 13. The compounds disclosed by Brooks necessarily comprise a mutilin component for antimicrobial activity (see page 1, lines 35-38 and page 2, lines 4-9). Nowhere does Brooks disclose fused bicyclic compounds. Applicant submits that the amended claims are novel with regards to Brooks because the compounds and methods recited in the amended claims are vastly different from Brooks. Applicant further notes that the dependent claims are not anticipated at least by virtue of their dependency.

The Examiner objected to claims 1-4, 11-16, 21-23 and 26-29 under paragraph 28.2(1)(a) of the *Patent Act* alleging that the subject-matter defined by the claims was disclosed by Suling et al. ("Suling") more than one year before the filing date of the present patent application.

Applicant respectfully requests reconsideration and withdrawal of the anticipation objection for the following reasons.

Claims 12 and 13 have been cancelled, thus rendering the objection moot with respect to these claims.

Suling does not disclose compounds as recited in the amended claims. Claims 1, 21 (now 18) and 27 (now 24) have been amended to include the structural limitations of claim 13, with X₄ no longer including amino. The compounds disclosed by Suling have a 5-amino substituent that at least distinguishes them from the compounds recited in the amended claims. Furthermore, compounds 1, 3, 5, 7 and 11 are disclosed by Suling as being inactive against *M. tuberculosis*. Suling defines an active compound as having an MIC of less than or equal to 12.8 mg/L, whereas compounds 1, 3, 5, 7 and 11 of Suling all exhibit MIC values of greater than 12.8 mg/L. Applicant therefore submits that the amended claims are novel over Suling. Applicant further notes that the dependent claims are novel at least by virtue of their dependencies.

The Examiner has objected to claims 1-4, 11, 13, 17, 18, 20-23 and 26-29 under paragraph 28.2(1)(a) alleging that the subject-matter defined by the claims was disclosed by Leung et al. ("Leung") more than one year before the filing date of the present patent application.

Claims 13 and 18 have been cancelled, thus rendering the objection moot with respect to these claims.

Claims 1, 21 (now 18) and 27 (now 24) have been amended as aforementioned. Leung discloses the compound SRI-7614, which at least distinguishes the Leung compounds from the compounds recited in the amended claims.

Claim 20 (17) has been amended to no longer include the compound (1-Amino-8-phenyl-6,7-dihydro-5H-2,5,9-triazabenzocyclohepten-3-yl)-carbamic acid ethyl ester. Thus, the compounds in the amended claims are distinguished from SRI-7614.

Applicant therefore submits that the amended claims are novel over Leung. Applicant further notes that the dependent claims are novel at least by virtue of their dependencies.

The Examiner objected to claims 1-4, 11 and 21-23 under paragraph 28.2(1)(b) of the *Patent Act* alleging that Cho et al. ("Cho") disclosed the claimed subject matter before the claim date.

Claims 1 and 21 (now 18) have been amended as aforementioned. Conversely, the compounds disclosed by Cho are not bicyclic compounds, and thus are quite different from the compounds recited in the amended claims. Furthermore, compounds 4, 8, and 10-16 disclosed by Cho and cited by the Examiner are synthetic intermediates (see Scheme 1 and Scheme 2). Cho does not disclose that compounds 4, 8, and 10-16, in themselves, possess antibacterial activity, nor does Cho disclose methods for using these compounds against bacterium. Applicant therefore submits that the amended claims are novel over Cho and that the dependent claims are not anticipated at least by virtue of their dependency.

The Examiner objected to claims 1-3, 11, 13-18, 20-22 and 26 under paragraph 28.2(1)(b) of the *Patent Act* alleging that Didier et al. ("Didier") discloses the claimed subject matter before the claim date.

Claims 13 and 18 have been cancelled, thus rendering the objection moot with respect to these claims.

Claims 1 and 21 (now 18) have been amended as aforementioned. The compounds disclosed by Didier have a 5-amino substituent, which at least distinguishes the Didier compounds from the compounds recited in the amended claims. Furthermore, Didier does not disclose methods of using SRI-7462 and SRI-7614 against bacterium, nor do they disclose any antibacterial properties of these compounds. Rather, disclosed are methods directed toward the eradication of the microsporidia, *Encephalitozoon intestinalis*, which is not a bacterium. Applicant submits that the amended claims are novel over Didier, because Didier does not disclose compounds as recited in the present claims or method of using

them as antibacterial agents. Applicant further notes that the dependent claims are inventive at least by virtue of their dependencies.

Reconsideration and withdrawal of Examiner's objections under paragraph 28.2(1)(a) and paragraph 2.8.2(1)(b) of the *Patent Act* is respectfully requested.

Objection under Section 84 of the Patent Rules

The Examiner has objected to claims 1-19, 21-35 and 37-42 under Section 84 of the *Patent Rules* based on the allegation that the claims are broader in scope than the teaching of the description. More specifically, the Examiner asserts that the compounds of the claims be limited to when S₁ (R₁) is methyl, ethyl, phenyl and benzyl.

Claims 12, 13 and 18 have been cancelled, thus rendering the objection moot with respect to these claims.

Claims 1, 14 (now 12), 16 (now 14), 19-21 (now 16-18), 27 (now 24) and 37 (now 34) have been amended to comprise compounds corresponding to Formula II in the description, with S₁ (R₁) being an organic radical comprising 1 to 8 carbon atoms.

The description discloses that S₁ (R₁) can be an "organic radical which includes but is not limited to an alkyl group or a lower alkyl group" (p.28, lines 15-16). The description also discloses that S₁ (R₁) can be an organic radical comprising from 1 to 8 carbons (p. 13-14). Thus, the specification provides verbatim support for the recitation of S₁ (R₁) being "an organic radical comprising from 1 to 8 carbon atoms."

Furthermore, the recitation of "an organic radical comprising from 1 to 8 carbons" is not an unreasonable or unsupported limitation. The specification describes structure-activity relationships regarding substitution at S₁ (R₁). Specifically, Table 4 provides that if S₁ (R₁) of Region A is a long chain or bulky aliphatic group, then activity against Mammalian Tubulin is reduced, but larger steric groups can be tolerated at this position during the inhibition of bacterial growth.

Thus, the skilled artisan would fairly glean from the specification that longer and bulkier organic chains at S₁ (R₁) (*i.e.*, chains other than methyl, ethyl, phenyl, and benzyl) can reasonably be expected to have activity.

Moreover, the Examiner's assertion that there is a lack of support for compounds other than those with S₁ (R₁) being methyl, ethyl, phenyl and benzyl, is incorrect. The specification provides the specific examples of A11, wherein S₁ (R₁) is *s*-butyl, and A184, wherein S₁ (R₁) is *n*-chloroethyl. The specification also teaches that larger alkyl groups at S₁ (R₁) can be tolerated, specifically "*n*-butyl and *t*-butyl" (p. 38, lines 5-10). Therefore, reconsideration and withdrawal of Examiner's objection under Section 84 of the *Patent Rules* is respectfully requested.

Objection under Section 2 of the Patent Act

The Examiner has objected to claims 1-42 under Section 2 of the *Patent Act* based on the allegation that it is being directed to a medical treatment that does not produce an essentially economic result.

Claims 12, 13 and 18 have been cancelled, thus rendering the objection moot with respect to these claims.

Claims 37-42 (now 34-39) have been amended and are now directed to "use" type claims, which are believed to be allowable under current patent practice.

With respect to claims 1-11, 14-17 and 19-33, Applicant respectfully submits that these claims are not directed to a method of medical treatment, and therefore do recite patentable subject matter. The amended claims address methods for inhibiting bacterial growth (independent claims 1, 20 (now 17) and 36 (now 33)), a method of killing bacteria (independent claim 21 (now 18)), and a method of inhibiting FtZ polymerization in bacteria (claim 27 (now 24)). Applicant notes that these methods are not directed to a medical treatment. For example, the specification describes that the compounds can be used for "purification of water (this can include municipal water, sewage treatment systems, potable and non-

potable water supplies, and hatcheries, for example)" (p. 25, lines 12- 15). Applicant therefore submits that the methods recited in claims 1, 20 (now 17) claim 21 (now 18), claim 27 (now 24) and 36 (now 33) produce an essentially economic result in relation to trade, commerce or industry. Claims 2-11, 14-17 (now 12-15), 19-20 (now 16-17) are dependent on claim 1, and claims 22-26 (now 19-23) are dependent on claim 21 (now 18), claims 28-35 (now 25-32) are dependent from claim 27 (now 24) and thus are also within the definition of "art", at least by virtue of their dependencies. Applicant therefore respectfully requests reconsideration and withdrawal of the Examiner's objection to these claims under section 2 of the *Patent Act*.

Objections under subsection 27(4) of the *Patent Act*

The Examiner has objected to claims 1, 12-19, 21, 27 and 37 under subsection 27(4) of the *Patent Act* as being ambiguous based on the allegation that the term "or" before the last element in a specified group causes a lack of clarity.

Claims 12, 13 and 18 have been cancelled, thus rendering the objection moot with respect to these claims.

Claims 1, 14-17 (now 12-15), 19 (now 16), 21 (now 18), 27 (now 24) and 37 (now 34) have been amended to replace the term "or" with the term "and" before the last element in a specified group.

Reconsideration and withdrawal of Examiner's objection under subsection 27(4) of the *Patent Act* is respectfully requested.

The Examiner has objected to claims 1, 12-14, 16-19, 21, 27 and 37 under subsection 27(4) of the *Patent Act* as being indefinite based on the allegation that the expression "organic radical comprising 1-8 (26) carbon atoms" is open-ended.

Claims 12, 13 and 18 have been cancelled, thus rendering the objection moot with respect to these claims.

With respect to claims 1, 14, 16, 17, 19, 21, 27 and 37, Applicant respectfully disagrees that the expression "organic radical comprising 1-8 (26) carbon atoms" is open-ended. Applicant submits that the expression "organic radical comprising 1-8 (26) carbon atoms" is not open-ended, as lower and upper bounds for the number of carbon atoms are provided. The scope of the claims is possible to determine with ease. For example, given a selection of a carbon number and a degree of unsaturation, molecular formulas and structural formulas can be readily ascertained. So if an organic radical comprises 3 carbons and is saturated, then molecular formulas of C_3H_8 (*i.e.* $C_nH_{(2n+2)}$) as well as substituted analogues, $C_nH_{(2n+2-x)}R_x$ (*e.g.* C_3H_7Cl) and any structural isomers thereof are possible organic radicals. Thus, one of skill in the art, after the selection of a carbon number, a degree of unsaturation, and any substitution, can readily ascertain the precise structural formula of an organic radical. Given the fact that finite number of chemical possibilities exist and that upper and lower bounds restrict the possibilities sufficiently, it is impossible for the claim language to be open-ended and/or indefinite. Furthermore, such claim language is reasonable in light of the diversity of organic radicals comprising 1-8 (26) carbons atoms specifically disclosed in Table 8 and in light of the detailed structure activity relationships outlined in Table 4. Applicant therefore respectfully requests reconsideration and withdrawal of the Examiner's objection to claims 1, 14, 16, 17, 19, 21, 27 and 37 under subsection 27(4) of the *Patent Act*.

The Examiner has objected to claim 11 under subsection 27(4) of the *Patent Act* based on the allegation that the term "about" causes ambiguity.

Claim 11 has been amended to remove the term "about".

Reconsideration and withdrawal of Examiner's objection to claim 11 under subsection 27(4) of the *Patent Act* is respectfully requested.

Other Objections

The Examiner has objected to claim 15 under subsection 87(2) of the *Patent Rules*, asserting that depend claims must refer to preceding claims.

Claim 15 (now 13) has been amended to depend on claim 14 (now 12).

Reconsideration and withdrawal of Examiner's objection to claim 15 under 87(2) of the *Patent Rules* is respectfully requested.

Disclosure page 1, lines 5-6 have been amended to remove the references to government support.

Applicant submits herewith an amended Figure 3 in response to Examiner's request.

Applicant has amended pages 11, 12, 21, 23, 39, 40 and 44 to delete all reference to incorporation by reference, in response to the Examiner's objection under the subsection 81(1) of the *Patent Rules*.

We trust that, with the above amendments, this application is now in a form acceptable for favourable consideration by the Examiner.

Early and favorable consideration of this application is respectfully requested.

In the event that this application is currently deemed to be abandoned for failure to pay any prescribed fee, or for any other reason, the applicant requests reinstatement of this application. Accordingly, the Commissioner is requested and authorized to deduct the prescribed reinstatement fee of \$200.00 for each cause of abandonment and any other fees currently due, directly from our account number 600000771.

Respectfully submitted,

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Encl. Disclosure pages 1, 11, 12, 21, 23, 39, 40 and 44
Claim pages 93-119
Figure 3, page 3/9